REMARKS

Claims 1-67, 69-79, 81-86, and 88-96 remain in the application. Claims 1, 27, 30, 31, 34, 40, 44, 67, 72, 77, 78, 82, 88, 95, and 96 are amended and claim 68 is canceled (claims 80 and 87 were previously canceled).

Claims 30, 32, 34, 44, 72, 77, 78, and 82 are objected to because of several informalities.

The Examiner indicates that claim 30 states the use of at least one drug, medicament, vitamin, mineral or controlled dietary matter or content is utilized, but that independent claim 1 states that a drug, medicament or controlled dietary content is not required.

Claim 1 does not require that a drug, medicament or controlled dietary content be used. However, such items ***may*** be used to further enhance the acoustic or vibration energy. Claim 1 is amended to clarify the optional use of such items and to recite the same items as claim 30, namely, drug, medicament, vitamin, mineral or ingested dietary matter or content, and claim 30 is amended to refer to these items recited in claim 1. Claims 31, 34, 40, and 44 are amended to be consistent with amended claim 1. Such amendments are considered to obviate the objection to claims 30 and 32 and to respond to the Examiner's invitation to inspect other claims for similar incidences. Thus, Claim 1 recites the optional use and claims 30 and 32 recite the use.

Claim 34 recites two alternatives: either the drug, medicament, vitamin, mineral or ingested dietary content reaches the brain in unaided form or it reaches the brain in aided form. If in aided form, then options (a), (b), (c), or (d) may be employed. Applicants see no irrelevancy to reciting that one approach (unaided) or the other (aided) is recited in the same claim as "either-or", and the Examiner has cited no basis, statutory or otherwise, to support his objection.

Claim 44, which is objected to under 37 CFR 1.75(c) should now be proper, since claim 1 has been amended to recite that the therapy optionally employs a drug, medicament or controlled dietary matter or content, whereas claim 44 indicates that these items need not be used. Thus, there are two cases, one not requiring the use of these items, and one requiring the use of these items. Claim 1 states that the use is optional, and

claims 30 and 32 positively recite the use of these items, while claim 44 recites the non-required use. Claim 44 is also amended to be consistent with amended claim 1. Applicants see no basis to object to an independent claim reciting optional use and to dependent claims separately directed to use and non-use, and the Examiner has provided no support, statutory or otherwise, for such a position.

The Examiner suggests that claim 72 should read "The system of claim 1, wherein at least one of ...". Applicants agree and have so amended claim 72.

The Examiner points out some inconsistencies in the wording of claim 77. Applicants have amended the language in claim 77 to read "acoustic and vibration emitter" and "acoustic and vibration energy", to be consistent with the language used in claim 1.

Claim 82 is amended to depend from claim 1, rather than canceled claim 80.

Reconsideration of the objection of claims 30, 32, 34, 44, 72, 77, 78, and 82, as amended, is respectfully requested.

Claim 67 is rejected under 35 USC 101 as being directed to non-statutory subject matter, on the basis that the claim is directed to the removal of a nodule from the body by natural body processes.

Claim 67 is amended to incorporate the limitations of claim 68, which is accordingly canceled. Since claim 68 depended from claim 67 and was not rejected, this action should obviate the rejection.

Reconsideration of the rejection of claim 67, as amended, under 35 USC 101 is respectfully requested.

Claims 27-29, 78, and 88-94 are rejected under 35 USC 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicants regard as the invention.

The Examiner suggests amending the language of claim 27 to recite "is diagnosed to be at least one of". Applicants have amended claim 27 in a manner that they believe is consistent with the Examiner's suggestion.

The Examiner considers that claim 78 does not positively claim beam-forming or beam-steering. Applicants have amended claim 78 to positively recite beam-forming or beam-steering means.

The Examiner objects to the word "optional" in the claim. Applicants have amended claim 88 to delete the word.

Reconsideration of the rejection of claims 27-29, 78, and 88-94, as amended, under 35 USC 112, second paragraph, is respectfully requested.

Claims 1-4, 6, 11-16, 20-27, 30-32, 37-38, 44, 50-53, 56, 58, 60, 66, 71-73, 76, 78-79, 84, 86, 88-93, and 95-96 are rejected under 35 USC 103(a) as being unpatentable over Bystritsky (U.S. Patent 7,283,861).

Bystritsky discloses methods for modifying electrical currents in neuronal circuits, such as brain circuits through the simultaneous use of focused ultrasound pulse (FUP) and an existing brain-imaging system, such as functional magnetic resonance imaging (fMRI) system. The methods are used for research, treatment and diagnosis of psychiatric, neurological, and neuroendocrine disorders whose biological mechanisms include brain circuits. The methods include the simultaneous step of applying FUP to a live neuronal circuit within a brain and monitoring a brain image produced by a brain imaging system during the application of FUP.

Independent claims 1, 86, 88, 95, and 96 are reproduced below:

> 1. A system for the therapeutic treatment of abnormal protein-related or prion-related diseases of a human patient's brain or neurological system comprising:
>
> (a) acoustic exposure therapy means comprising at least one acoustic or vibration emitter for acoustically or mechanically coupling, directly or indirectly, acoustic or vibratory emissions into a brain or neurological region which has been, is, or is expected to potentially be subject to the nucleation, growth or deposition of abnormal-protein or prion-related deposits, nodules or bodies;
>
> (b) means for exciting said emitter to emit acoustic or vibration energy with a desired characteristic; and
>
> (c) said emitter adapted to deliver therapeutic acoustic or vibration energy, directly or indirectly, to at least one of said brain or neurological regions, the therapy designed to provide, enable or accelerate at least one of the following therapy processes:
>
> (i) physical breakup, breakdown, erosion, dispersion, disentanglement, de-aggregation, redistribution, dissolution, de-agglomeration, de-amalgamation or permeation of at least some said deposits, nodules or bodies,
>
> (ii) interference in, slowing of, or reversal of at least one physical, chemical, biological or genetic deposit, nodule or body formation-process, formation-sequence or formation pathway anywhere in the process, sequence or pathway, and

(iii) aiding the recovery, growth, regrowth, new growth or improved chemical, physical, biological, genetic or cognitive functionality of brain-related or neurological-related cells, physiology or functional pathways negatively impacted or stressed by the deposition of, formation of, or presence of said deposits, nodules or bodies or their associated formation processes;

wherein said acoustic or vibration energy is capable of providing, enabling, accelerating or initiating said breakup, interference or aiding process, said acoustic or vibratory therapy process optionally employing a drug, medicament or controlled dietary content to proceed at a useful pace or to a useful extent.

86. A method for the therapeutic treatment of abnormal protein-related or prion-related diseases of a human patient's brain or neurological system comprising:

(a) acoustically coupling said patient's brain or neurological system to acoustic therapy means comprising at least one acoustic or vibration emitter for acoustically or mechanically coupling, directly or indirectly, acoustic or vibratory emissions into a brain or neurological region which has been, is, or is expected to potentially be subject to the nucleation, growth or deposition of abnormal-protein or prion-related deposits, nodules or bodies;

(b) exciting said emitter to emit acoustic or vibration energy with a desired characteristic; and

(c) delivering therapeutic acoustic or vibration energy from said emitter, directly or indirectly, to at least one said brain or neurological region, the therapy designed to provide, enable, accelerate or initiate at least one of the following therapy processes:

(i) physical breakup, breakdown, erosion, dispersion, disentanglement, de-aggregation, redistribution, dissolution, de-agglomeration, de-amalgamation or permeation of at least some said deposits, nodules or bodies,

(ii) interference in, slowing of, or reversal of at least one physical, chemical, biological or genetic deposit, nodule or body formation-process, formation-sequence or formation pathway anywhere in the process, sequence or pathway, and

(iii) aiding the recovery, growth, regrowth, new growth or improved chemical, physical, biological, genetic or cognitive functionality of brain-related or neurological-related cells, physiology or functional pathways negatively impacted or stressed by the deposition of, formation of, or presence of said deposits, nodules or bodies or their associated formation processes;

wherein a drug, medicament or controlled dietary content optionally being administered enhances therapy effectiveness or comfort, independently or in cooperation with the emitted energy.

88. A system for the therapeutic treatment of abnormal protein-related or prion-related diseases of a human patient's brain or neurological system comprising:

(a) means to direct acoustic or vibrational energy into or through at least one such diseased or potentially diseased anatomy portion; and

(b) a drug, medicament or controlled dietary content capable of contributing to the therapy also directly or indirectly delivered to the portion,

wherein the acoustics and optional drug together at least slow a cognitive loss process by slowing , stopping or reversing a deposition process; and wherein said optional drug enhances the therapeutic treatment over the acoustics alone in said portion.

95. A method of at least temporarily slowing, stopping or avoiding a patient's cognitive losses associated with a neural deposition disease, said neural deposition disease comprising any of abnormal protein-related or prion-related diseases, said method comprising administration of acoustic or vibrational energy into affected or potentially affected patient anatomy portions, said energy altering, blocking or reversing a cognitively-damaging deposition process, at least temporarily.

96. A system for at least temporarily slowing, stopping or avoiding a patient's cognitive losses associated with a neural deposition disease, said neural deposition disease comprising any of abnormal protein-related or prion-related diseases, said method comprising administration of acoustic or vibrational energy controllably emitted from an acoustic emitter into affected or potentially affected patient anatomy portions, said energy altering, blocking or reversing a cognitively-damaging deposition process, at least temporarily, wherein the system is used with a drug that enhances the slowing, stopping or avoiding in said portions.

Bystritsky teaches a way of stimulating/altering live neuronal circuits and then imaging them such as by using fMRI (fMRI is functional MRI vs. nonfunctional MRI) The "function" is electrical function in the brain neurons. MRI itself sees pathology and specifically not electrical function.

Bystritsky is specifically intentionally targeting live neuronal circuits, and at no point, directly or indirectly, says or implies that a deposition or deposition-process is addressed, or even that deposition patients are treated. Note that depositions are plaques which themselves ***have no electrical activity***. They are electrically inactive electrical insulators. Plaques therefore have no electrically functional activity that can be imaged

using fMRI or any other functional imaging tool. Applicants direct their ultrasonic stimulation/alteration to electrically inactive plaques, which would certainly be considered a 100% failure for Bystritsky's method. Most clearly, Bystritsky is teaching away from Applicants' invention, as he is specifically and purposely aiming at different targets (live neuronal circuits) for different reasons (to modify electrical currents therein).

Also note that Bystritsky's method is a two-step method involving FUP alteration/stimulation and temporally separate but near-simultaneous imaging. Applicants' invention, addressing deposition interdiction instead, does not require simultaneous imaging. In fact, Applicants' invention might even be employed to interdict plaque or plaque activity based on a previously taken MRI of where the plaque is located. Thus, for Applicants' invention, real-time imaging is not necessarily required. And further, Applicants can utilize MRI (vs. fMRI) to locate the plaques, whereas Bystritsky's method cannot use MRI as it cannot functionally image his different functional electrical targets. Thus, Applicants do not require functional imaging whereas Bystritsky does.

In any event, Bystritsky is going after different targets of a fundamentally different nature using a fundamentally different tool set. His targets are desirable neuronal circuits, while Applicants' targets are undesirable electrically inactive plaques. His method would not serve at all to interdict plaques and would not even be plaque-aware. Applicants' method and system does.

Finally, it is noted that Bystritsky says essentially nothing about how the ultrasound interacts with its target, i.e., shear-stress, compressional stress, etc. He never discusses or teaches acoustic mechanisms for altering plaques. He does not even discuss acoustic mechanisms for affecting his electrically active neurons! This clearly also says he did not have plaques in mind.

The Examiner cites disorders such as Parkinsonian Disease, among others, as examples of neurological disorders subject to research, treatment and diagnosis (Col. 1, lines 25-45). However, Bystritsky specifically discusses abnormalities in Cortico-Talamic-Straitum Circuit in connection with Parkinsonian Disease. Applicants' independent claims 1, 86, and 88 all recite "abnormal protein-related or prion-related diseases". There is no disclosure or suggestion in Bystritsky that abnormalities in Cortico-Talamic-Straitum Circuit involve abnormal protein-related or prion-related diseases. Independent claims 95

and 96 have been amended to recite the same limitation of "abnormal protein-related or prion-related diseases".

The Examiner states that the methods of Bystritsky "can be used to aid in the recovery, growth, regrowth, new growth or improved physical, biological and cognitive functionality of brain-related or neurological-related cells, or functional pathways negatively impacted or stressed by **deposits, nodules or bodies**" (Office Action, page 5; emphasis added). However, the Examiner provides no citation to this statement, and Applicants can not find any mention of deposits, nodules or bodies in Bystritsky. As recited earlier in claim 1, for example, such deposits, nodules or bodies are the consequence of the nucleation, growth or deposition of abnormal-proteins or are prion-related.

"To establish prima facie obviousness of a claimed invention, all the claim limitations must be taught or suggested by the prior art." *In re Royka*, 490 F.2d 981, 180 U.S.P.Q. 580 (CCPA 1974). M.P.E.P. § 2143. Accord, M.P.E.P. § 706.02(j). For at least these reasons, the rejection of claims 1-4, 6, 11-16, 20-27, 30-32, 37-38, 44, 50-53, 56, 58, 60, 66, 71-73, 76, 78-79, 84, 86, 88-93, and 95-96 based on Bystritsky should be reconsidered and withdrawn.

Reconsideration of the rejection of claims 1-4, 6, 11-16, 20-27, 30-32, 37-38, 44, 50-53, 56, 58, 60, 66, 71-73, 76, 78-79, 84, 86, 88-93, and 95-96, as amended, under 35 USC 103(a) as being unpatentable over Bystritsky is respectfully requested.

Claims 1, 7-10, 17-19, 27-29, 30, 33-36, 39-43, 47-49, 57, 59, 62-70, 73-74, 77, 79, 81-83, 85-86, 88-90, and 94-96 are rejected under 35 USC 103(a) as being unpatentable over Wallace (U.S. Patent 7,286,879) in view of Shalev et al (U.S. Patent Publication No. 2003/0176892; hereinafter "Shalev").

Wallace discloses a method of stimulating the fastigium nucleus to treat neurological disorders (such as acute stroke). The method comprises introducing an electrical stimulation lead within a patient's head, advancing the stimulation lead within an intracranial vascular body, such as a blood vessel or ventricle, placing the stimulation lead adjacent the fastigium nucleus of the patient's brain, and stimulating the fastigium nucleus with the stimulation lead to treat the neurological disorder.

Shalev discloses the administration of anti-inflammatory drugs into the central nervous system. Apparatus is provided for delivering a Non Steroidal Anti-Inflammatory

Drug (NSAID) supplied to a body of a subject for delivery to at least a portion of a central nervous system (CNS) of the subject via a systemic blood circulation of the subject, including a stimulator adapted to stimulate at least one site of the subject, so as to cause an increase in passage of the NSAID from the systemic blood circulation across a blood brain barrier (BBB) of the subject to the portion of the CNS, during at least a portion of the time that the NSAID is present in the blood, the site selected from the list consisting of: a sphenopalatine ganglion (SPG) of the subject, an anterior ethmoidal nerve and a retro-orbital branch of an SPG of the subject, a communicating branch between an anterior ethmoidal nerve and a retro-orbital branch of an SPG of the subject, a greater palatine nerve of the subject, a lesser palatine nerve of the subject, a sphenopalatine nerve of the subject, a communicating branch between a maxillary nerve and an SPG of the subject, a nasopalatine nerve of the subject, a posterior nasal nerve of the subject, an infraorbital nerve of the subject, an otic ganglion of the subject, an afferent fiber going into the otic ganglion of the subject, an efferent fiber going out of the otic ganglion of the subject, a vidian nerve of the subject, a greater superficial petrosal nerve of the subject, and a lesser deep petrosal nerve of the subject.

Independent claims 1, 86, 88, 95, and 96 are set forth above.

The Wallace reference (the primary reference) on its face has a filing date of **July 16, 2004**, which is ***later*** than Applicants' non-provisional filing date of **July 1, 2003**. Since the primary reference is filed ***after*** Applicants' application, then the rejection must fall.

However, in the event that there is something Applicants' undersigned representative missed, an analysis of Wallace and Shalev is given below.

Wallace teaches a method of ***electrically*** stimulating a specific brain portion (the FN or fastigium nucleus) which, ***in turn***, induces an increase in blood flow elsewhere. An increase in blood flow is known to be desirable in many neurological conditions. Note that what is being stimulated is a first brain segment which, in turn, appears to reduce inflammation and increase blood flow at second locations away from that portion. In other words a helpful natural process is being instigated at point A (the FN) to help at point(s) B (e.g., an infarct, etc.). Apparently, the FN produces a beneficial enzyme or hormone which increases blood flow.

In any event, depositions are not directly targeted by incoming energy of any sort, as in Applicants' claimed invention. They are not targeted at all in the Wallace method. Further, plaques cannot be electrically stimulated by the Wallace method, as they are electrical insulators.

Any relevance of Wallace's invention is merely that it increases blood flow which can, in turn, possibly have indirect benefits to various neural diseases. Wallace suggests increased blood flow increases metabolism of plaques. Research to date, however, suggests that any help from increased blood flow comes from it reducing the average concentration of plaque precursors in the cerebrospinal fluid (CSF). This is a preventative measure as well, as opposed to a reversal of an existing deposition.

In any event, Wallace does not treat depositions or deposition regions with energy or fields directed into those regions, the field or energy itself ***directly*** acting upon a deposition.

There are long-known methods of inducing increased blood flow using drugs and heat or warmth. These would cause the same beneficial effect and likewise are only indirectly beneficial to some neural diseases.

Furthermore, Wallace is not only treating a first tissue portion to gain a benefit at a second. He also states that his electrode need only be within 2-30 mm of the first portion. So his FN electrical pulses are not only ***not*** applied directly to neurally damaged tissue but are even indirectly applied to his first portion of tissue as well.

There is nothing in Wallace that would lead one to ***directly*** attack or interdict a plaque or plaque making process with acoustical energy directed to that plaque portion. Applicants' invention *does not require FN stimulation or any other electrical stimulation of any tissue anywhere to work.*

No method, Wallace's or any other, that indirectly increases blood flow in a neurally diseased region will lead one skilled in this art to Applicants' method which (differently) does not target the manipulation of blood flow, does not target a first tissue portion while trying to actually treat a second portion, does not electrically stimulate anything, and directly targets and attacks plaques without requiring increased blood flow.

Wallace can certainly also be argued as teaching away from Applicants' claimed invention because he uses his therapeutic pulses at (or only near) the first tissue por-

tion to activate the body to come to its own defense at a second location(s). In contrast, Applicants use their energy to directly go after plaques where they or their formation process is located. Wallace makes no inference or suggestion that his electrical pulses-***even if they were applied directly to plaques*** (which he does not suggest) would remove or reverse plaque or plaque formation. No direct or indirect electrical / plaque dissolution mechanisms are taught or suggested as even being possible.

Applicants' claimed invention recites the directed (and direct) treatment of the depositions with mechanisms that attack plaques directly. Wallace teaches no directed treatment, no direct treatment, no delivered-energy attack upon plaques and no acoustics impinging upon plaque deposits.

Shalev, like Wallace above, involves treating a first portion (MST site) such that the separate treatment of a second diseased portion becomes possible. All treatment energy sources Shalev discusses are used to open the BBB at one of Shalev's MST sites such that a systemic intravenous NSAID drug can enter the brain from the blood stream at and ***through*** the MST site.

The Shalev energy sources do not treat the diseased tissue in the brain; the NSAIDS do that. The Shalev energy sources (including ultrasound) are used solely to open up the BBB for subsequent delivery of a systemic NSAID drug. Shalev does not infer or suggest provision of an energy source directable to diseased tissue and offering a plaque dissolution or inhibition mechanism.

Therefore again, not taught here is any use of any energy to directly attack a plaque. Thus, Shalev in combination with Wallace fails to disclose or even remotely suggest Applicants' claimed invention.

The Jolesz reference that Shalev cites teaches the same thing, namely, the use of ultrasound to open the BBB (and to verify its acoustic opening via ultrasound imaging of the BBB). The detailed list of modulation target sites (MSTs) taught by Shalev are merely useful potential drug ports in the BBB and NOT sites of plaque deposition.

"To establish prima facie obviousness of a claimed invention, all the claim limitations must be taught or suggested by the prior art." *In re Royka*, 490 F.2d 981, 180 U.S.P.Q. 580 (CCPA 1974). M.P.E.P. § 2143. Accord, M.P.E.P. § 706.02(j). For at least these reasons, the rejection of claims 1, 7-10, 17-19, 27-29, 30, 33-36, 39-43, 47-49, 57,

59, 62-70, 73-74, 77, 79, 81-83, 85-86, 88-90, and 94-96 based on Wallace in view of Shalev et al should be reconsidered and withdrawn.

Reconsideration of the rejection of claims 1, 7-10, 17-19, 27-29, 30, 33-36, 39-43, 47-49, 57, 59, 62-70, 73-74, 77, 79, 81-83, 85-86, 88-90, and 94-96, as amended, under 35 USC 103(a) as being unpatentable over Wallace (U.S. Patent 7,286,879) in view of Shalev et al is respectfully requested.

Applicants provide the following additional comments for the Examiner's consideration.

Reading Bystritsky would lead one away from even trying to deal with plaques directly, as they are not electrically active and cannot be functionally imaged.

Likewise, Wallace utilizes an indirect scheme where any of his applied energy never has to arrive at a plaque location. Further, his energy does not directly treat the disease.

Likewise, Shalev, although offering a new invasive way of opening the BBB using energy of several types, also treats brain disease indirectly, not using the energy but using a systemic drug deliverable because of the energy being applied elsewhere. Ultrasound had been previously used to open the BBB.

These three references certainly collectively and individually teach away from direct interdiction of plaques with an energy source such as an acoustic directed energy source. Acoustic energy-levels necessary to dissolve, obliterate or break-up plaques will likely damage or kill viable neurons if aimed at them so Applicants' invention again is not inferred or suggested by Bystritsky's gentle stimulation FUPs. Of course, Bystritsky does not even mention such deposits. Bystritsky also does not disclose or suggest imaging plaques; thus, he would not be able to aim at them anyway, nor even know where they are.

Bystritsky does not mention Alzheimer's, depositions or plaques. Wallace mentions plaques but suggests that increased blood flow will metabolize them. Applicants know of no such data and even if it existed, their other arguments of that invention's irrelevance to their invention hold. Shalev cites a provisional patent of his relating to Alzheimer's treatment; however, this is again for treatment WITH NSAIDS.

Applicants note that claims 5, 54, 55, and 75 have not been rejected over cited art, although the Examiner does not appear to acknowledge this. Thus, these claims should be allowable.

The Examiner indicates that claims 45, 46, and 61 would be allowable if rewritten in independent form, including all of the limitations of the base claim and any intervening claims.

Applicants appreciate that these claims are allowable. However, for the reasons given above, the remaining claims in the application are also considered to be patentable.

Specifically, based on the fact that Wallace was filed after the instant application, then at least claims 7-10, 17-19, 28-29, 33-36, 39-43, 47-49, 57, 59, 62-65, 67-70, 74, 77, 81-83, 85, and 94 should also be allowable. This list comprises those claims rejected over the combination of Wallace and Shalev and not rejected by Bystritsky. Of course, Applicants also submit that the claims rejected over Bystritsky are also allowable for the reasons given.

The foregoing amendments and arguments are submitted to place the application in condition for allowance. The Examiner is respectfully requested to take such action. If the Examiner has any questions, he is invited to contact the undersigned at the below-listed telephone number.

Respectfully submitted,

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